

Q17 of the mouse SMAD6 gene (Imamura et al., 1997, *Nature* 389: 622-626). The rchd534-long sequence was reported in Hata et al., 1998, *Genes and Development* 12: 186-197.

IN THE CLAIMS

Please cancel Claims 14-25 and 29-33, without prejudice to the subject matter therein.

Please amend the claims as follows.

1. (Once Amended) A homozygous transgenic animal having a mutated rchd534 gene, wherein the wild-type rchd534 gene has been replaced with a rchd534-LacZ gene which lacks the MH2 domain encoding region, and wherein said animal displays a cardiovascular disease symptom.

Q18 2. (Once Amended) The transgenic animal of claim 1, wherein said cardiovascular disease symptom is hyperplasia, thickening of at least one cardiac valve, cardiac outflow tract development defects, cardiovascular calcification, epicardial vascular malformations, endocardial vascular malformation, or defects in the regulation of vascular tone.

3. (Once Amended) The transgenic animal of claim 1, wherein said cardiovascular disease symptom is cardiovascular calcification.

4. (Once Amended) The transgenic animal of claim 1, wherein said cardiovascular disease symptom is aortic or valvular calcification.

Q19 6. (Once Amended) A cell having a mutated rchd534 gene isolated from the transgenic animal of claim 1, wherein said cell is isolated from tissue displaying a cardiovascular disease symptom.

Q20 10. (Once Amended) A method of producing a homozygous transgenic animal having a mutated rchd534 gene, wherein the wild-type rchd534 gene has been replaced with a rchd534-LacZ gene which lacks the MH2 domain encoding region, comprising introducing a

Q 20 polynucleotide into an embryonic cell of said animal through homologous recombination with an endogenous rchd534 gene, and wherein said transgenic animal displays a cardiovascular disease symptom.

Q 21 26. (Once Amended) A method for identifying a substance for treating or preventing cardiovascular disease, comprising administering said substance to a homozygous transgenic animal having a mutated rchd534 gene, wherein the wild-type rchd534 gene has been replaced with a rchd534-LacZ gene which lacks the MH2 domain encoding region, wherein said transgenic animal displays a cardiovascular disease symptom, and wherein amelioration of said cardiovascular disease symptom indicates a substance effective in the treatment or prevention of cardiovascular disease.

2006/07/17 09:09:06